News from

The American Society for Cell Biology 48th Annual Meeting

San Francisco, CA
December 13–17, 2008

EMBARGOED FOR RELEASE
10:00 am, U.S. Pacific Time
Monday, December 15, 2008

Contact

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Author presents

Monday, December 15
5:25 pm
Minisymposium #13
Program #785
Imaging and Biosensors
Room 302, Moscone Center

Determining Spatial and Temporal Limits of the Tumor Intravasation Microenvironment In Vivo

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A small tumor is a large place

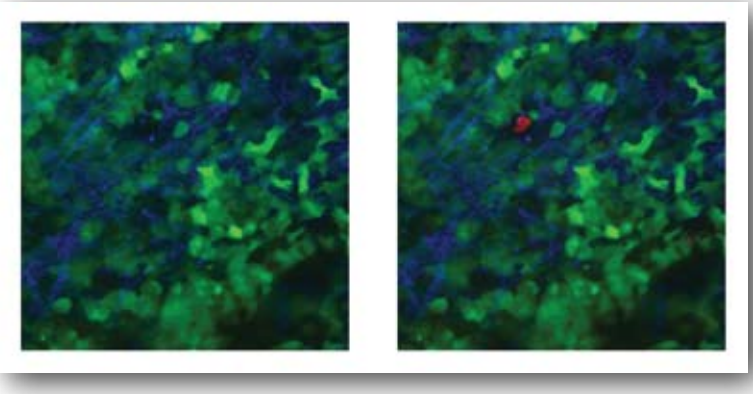
Throwing a "photoswitch" on cancer cells lights up the microenvironment and shows how tumor cells are guided toward a blood vessel

Small tumors are like minor surgery: If it's your surgery, it's not minor. If it's your tumor, it's not small. But increasingly, biologists are discovering that even a small tumor can be a large place and that a cell's location—its microenvironment—within a tumor can decide its fate. That's because cells are always signaling to each other. Figuring out what individual tumor cells are saying could tell researchers how to break up the cancer conversation.

But tracking single cells or even small groups in a tumor is difficult. Using the power of genetically inserted fluorescent marker proteins, scientists have had some success in tissue culture, but the tumor microenvironment in living creatures is much more complex—frustratingly so, say researchers at the Gruss Lipper Biophotonics Center at the Albert Einstein College of Medicine in New York. They now report a breakthrough technique that allows them to watch individually labeled tumor cells move about in real time and in a real mouse. Bojana Gligorijevic, Dmitry Kedrin, and Jacco van Rheenen, in the labs of Jeff Segall and John Condeelis, have been able to watch a tumor get organized over time through a special glass "window" inserted into the tumor in a mammary gland. The researchers marked cancer cells in the tumor with a green fluorescent protein and then bathed two small groups of cells in a blue laser, permanently "photoswitching" the green fluorescence to red. Through the window, the researchers followed the red-switched cancer cells as they grew and moved about in reaction to their microenvironment.

Gligorijevic and her colleagues are interested in intravasation, the deadly process by which certain tumor cells invade the surrounding basal membrane and tap into blood vessels. In their experiment, the two red-switched cell populations were only five cell diameters apart in the tumor, but location made all the difference, Gligorijevic reports. One group was near a flowing blood vessel; the other, farther "inland" in the tumor. Twenty-four hours after the red markers were switched on, the team could see the cells near the vessel moving toward the blood supply. The number of marked cells decreased as they were launched into the blood vessel. Meanwhile, the inland cancer population had moved little but increased in number.

Gligorijevic says that they plan to focus on the differences between the two microenvironments, looking for the critical interactions that drive intravasation in one part of the tumor and not in the other. "Using this approach, we can now link the behavior of individual tumor cells to the type of microenvironment within the tumor, a classification which will help us in developing and testing microenvironment-specific drugs," Gligorijevic explains.



Tumor cells are constantly moving, with different speeds and directions. This makes it hard to predict their future position. By changing the color of one cell from green to red, we can recognize a tumor cell after it has been moving around in the tissue for days. In these images taken inside a living animal, we can see connective collagen fibers in blue, fluorescently marked normal cells in green, and tumor cells "photoswitched" to red.